REMARKS

Status of the Claims:

Claims 1-11 are pending. Claims 1, 4 and 9 have been amended to more particularly point out the invention. Support for these amendments can be found on page 2, lines 1-10; page 6, line 20 to page 7, line 20; and page 31, lines 20-21.

New claims 12-23 have been added to more particularly point out the invention. Support for these amendments can be found in the table below.

Claim	Support
claim 12	page 6, line 20-page 7, line 10
claim 13	page 6, line 20-page 7, line 10
claim 14	page 6, lines 15-19
claim 15	page 6, line 20-page 7, line 10 and page 45, lines 20-25
claim 16	page 6, line 20-page 7, line 20
claim 17	page 6, lines 26-28
claim 18	page 6, line 20-page 7, line 10
claim 19	page 6, line 20-page 7, line 10
claim 20	page 7, lines 6-10
claim 21	page 7, lines 6-10
claim 22	page 7, lines 6-10
claim 23	page 6, line 20-page 7, line 6

No new matter has been added by these amendments.

Anticipation Under 35 U.S.C. §102(b)

Claims 1-11 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Blazar et al. (WO 95/34320; hereafter "Blazar"). (Office Action at page 3-4). The standard required for finding anticipation under 35 U.S.C. § 102(b) mandates that each and every element as set forth in the claim be found, either expressly or inherently

described in a single prior art reference. MPEP § 2131. Blazar does not meet this standard.

The Office alleges that Blazar teaches the use of inhibitors including those that bind both B7-1 and B7-2 to induce T cell unresponsiveness for bone marrow transplantation, including its use for the treatment of haematological malignancies and anaemia. The Office also states that Blazar teaches that the inhibitory agents can be administered for 18-36 hours after T cell priming. Applicants respectfully point out that the Office has mischaracterized Blazar on page 4 of the Office Action (*See* Blazar page 23, lines 5-10). Blazar does not teach or suggest that inhibitory agents can be administered for 18-36 hours after T cell priming. Blazar discloses that the 18-36 hours is the duration of the priming step, not the inhibitor step. Nonetheless, without conceding the correctness of the rejection, and for the sole purpose of expediting prosecution, Applicants have amended to claim 1 to recite "the immunoglobulin specific to B7-2 can compete with the murine antibody 3D1 for binding to B7-2." Blazar does not disclose an immunoglobulin specific to B7-2 that can compete with the murine antibody 3D1 for binding to B7-2. Thus, Blazar does not anticipate claim 1 as amended herein. Claim 9, has been similarly amended and thus is not anticipated by Blazar. Claims 2-8 and 11 depend, either directly or indirectly, on claim 1. Claim 10 depends on claim 9. Applicants therefore respectfully submit that the rejection of claims 1-11 under 35 U.S.C. § 102(b) is obviated by these amendments.

Obviousness Rejection Under 35 U.S.C. § 103

Claims 1-11 stand rejected as being obvious in light of Blazar alone, or in combination with U.S. Patent No. 6,096,537 (hereinafter, "Chappel"), U.S. Patent No. 6,096,537 (hereinafter, "Dinsmore") and Goldberg et al. 1994, *Transplant Immunology* 2:27 (hereinafter, "Goldberg"). The Office alleges the claimed invention is rendered obvious by Blazar because Blazar allegedly discloses a 3-hour in vitro incubation step with non-antibody B7 inhibitors and additionally discloses B7 specific antibodies administered in vivo. The Office further alleges the claimed invention is rendered obvious by Blazar in light of Chappel, which teaches masking antigens through pretreatment prior to transplantation, with agents, such as antibodies, for 30 minutes to induce immunological non-responsiveness. The Office also alleges that Dinsmore and Goldberg support the position that the prior art provided sufficient motivation and expectation of success for administering, ex vivo, inhibitory antibodies that meet the time limitation of the instant claims. Applicants maintain that the rejection is in error and respectfully request that it be withdrawn.

The Claimed Invention Is Not Prima Facie Obvious

MPEP § 2143 provides the standard required to establish a prima facie case of obviousness. "First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references combined) must teach or suggest all the claim limitations."

The reasonable expectation of success must be found in the prior art, not in the applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). The references must be considered as a whole and must suggest the desirability, and thus the obviousness of making the combination. *Hodosh v. Block Drug Co., Inc.,* 786 F.2d 1136, 1143 n.5, 229 U.S.P.Q. 182, 187 n.5 (Fed. Cir. 1986); MPEP § 2141. The Patent and Trademark Office (PTO) bears the burden of initially establishing a prima facie case of obviousness. MPEP § 2142.

The PTO has not established that the claimed invention is prima facie obvious in light of the teachings of Blazar alone. Blazar does not teach or suggest all of the claim limitations. Chappel, Dinsmore and Goldberg add nothing to cure this defect.

The Invention Is Not Obvious In Light of Blazar Alone

Blazar neither discloses or suggests a method of transplanting cells which requires contacting the donor cells with an immunoglobulin specific to B7-1, an immunoglobulin specific to B7-2, wherein the immunoglobulin specific to B7-2 can compete with the murine antibody 3D1 for binding to B7-2. The claimed invention, as amended herein, is thus distinct from the method described in Blazar.

Blazar Combined With Chappel, Dinsmore and Goldberg

Blazar combined with Chappel, Dinsmore and Goldberg does not render the claimed invention obvious because the combined references do not teach or suggest all of the claim limitations. The combined references do not teach or suggest a method of transplanting cells which requires contacting the donor cells with an immunoglobulin

specific to B7-1, an immunoglobulin specific to B7-2, wherein the immunoglobulin specific to B7-2 can compete with the murine antibody 3D1 for binding to B7-2.

Blazar discloses methods of transplanting cells by contacting, ex-vivo, donor and recipient cells with CTLA4Ig or a B7-1 antibody or a B7-2 antibody and a second agent such as an LFA-1 antibody or an IL-2 receptor specific antibody. Blazar also discloses in vivo administration of B7-1 and B7-2 antibodies.

Chappel discloses a thirty minute in vitro pre-transplantation step where donor cells are incubated with a masking agent, such as an antibody which binds specifically to LFA-1, MHC I, or MHC II. Chappel specifically discloses transplantation of pancreatic islet cells. Chappel does not disclose B7-1 or B7-2 specific antibodies.

Like Chappel, Dinsmore also discloses targeting MHC I. Dinsmore also discloses targeting LFA-3. In Dinsmore, however, the target cell is a cardiomyocyte instead of a pancreatic islet cell. The cardiomyocytes are incubated with an MHC I specific antibody for 1 hour and then the cells are administered with cyclosporine, a potent immunosuppressive drug that has many deleterious side effects. Dinsmore does not disclose B7-1 or B7-2 specific antibodies.

Goldberg discloses targeting CD45 on the surface of hematopoietic cells contained within a whole porcine kidney. CD45 is a marker for all hematopoietic cells. In Goldberg, whole kidneys were removed from pigs and perfused with an anti-CD45 antibody that was labeled to visualize staining. A successful transplant was never even attempted. Goldberg does not disclose B7-1 or B7-2 specific antibodies.

The combined references do not teach or suggest an immunoglobulin specific to B7-2 that can compete with the murine antibody 3D1 for binding to B7-2. Because the cited references fail to teach or suggest all of the claim limitations, Applicants respectfully request withdrawal of the rejection of claims 1-10 under 35 U.S.C. §103.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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